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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/846,017	04/25/97	CECH	T 07681.0003

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EXAMINER	
MYERS,C	
ART UNIT	**PAPER NUMBER**
1655	29

DATE MAILED: 07/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/846,017	Cech et al
Examiner	**Group Art Unit**
Carla Myers	1655

☒ Responsive to communication(s) filed on *Apr 17, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *29* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *29* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *16, 22*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. The disclosure is objected to because of the following informalities:

In the section "Brief Description of the Drawings", the specification should be amended to refer to and describe each of the embodiments of the figures. See, for example, Figures 1Ab and 7A-7B.

2. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 29 is drawn to a method of detecting a polynucleotide encoding a human telomerase gene product wherein the method comprises contacting a sample containing a target nucleic acid with a probe and detecting the resulting probe/target nucleic acid complex or amplifying the target nucleic acid and detecting the amplification product wherein detection of said complex or said amplification product is indicative of the presence of a polynucleotide encoding a human telomerase. The specification teaches a single human telomerase cDNA which consists of the sequence of SEQ ID NO: 100 and teaches an EST consisting of SEQ ID NO: 62 which encodes for a fragment of a human telomerase protein. The specification does not disclose any additional polynucleotides encoding human telomerase. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded

that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of specifies have been described by their complete structure. In the instant case, only 1 member of the broadly claimed genus has been defined by its structure. The human telomerase protein is known to consist of four distinct subunits. The specification does not disclose polynucleotides encoding any additional subunits of the telomerase protein and does not disclose polynucleotides encoding any variants or mutants of the telomerase protein. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. restriction map, biological activity of an encoded protein product, etc.). In the instant case, no such identifying characteristics have been provided for any of the broadly claimed polynucleotides encoding

telomerase proteins or probes which specifically bind said polynucleotide or primers which amplify said polynucleotide. While at the time of filing applicants were in possession of polynucleotides consisting of SEQ ID NO: 100, the limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of a representative number of polynucleotides encoding telomerase or a representative number of probes or primers which specifically detect said polynucleotide. Therefore, Applicants have not provided sufficient evidence that they were in possession, at the time of filing, of the invention as it is broadly claimed and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Revised Interim Guidelines for Written Description set forth in the Federal Register, December 21, 1999. Vol. 64, No. 244, pages 71427-71440.

3. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for detecting a polynucleotide encoding a human telomerase gene product, wherein said polynucleotide consists of the sequence of SEQ ID NO: 100 and wherein said method comprises contacting a sample with a probe consisting of SEQ ID NO: 100, does not reasonably provide enablement for methods for detecting any polynucleotide encoding any human telomerase gene product. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 29 is drawn to a method of detecting a polynucleotide encoding a human telomerase gene product wherein the method comprises contacting a sample containing a target nucleic acid with a probe and detecting the resulting probe/target nucleic acid complex or amplifying the target nucleic acid and detecting the amplification product wherein detection of said complex or said amplification product is indicative of the presence of a polynucleotide encoding a human telomerase. The specification (pages 94-97) teaches a single human telomerase cDNA which consists of the sequence of SEQ ID NO: 100 and teaches an EST consisting of SEQ ID NO: 62 which encodes for a fragment of a human telomerase protein. The specification (Table 3) also teaches a number of primers derived from the sequence of SEQ ID NO: 62. While these primers are shown to be useful for amplifying nucleic acids comprising a portion of SEQ ID NO: 100, there is no evidence of record to indicate that these primers "specifically amplify" a polynucleotide encoding a human telomerase gene product, as is required by claim 29. The specification does not enable one of skill in the art to make and use a representative number of nucleic acids encompassed by the broad scope of the claims. That is, the identification of a single human polynucleotide encoding a subunit of the human telomerase protein does not enable one of skill in the art to make and use the vast number of possible human telomerase polynucleotides encompassed by the claims. Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims

must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the specification does not provide sufficient guidance as to how to use the single human telomerase cDNA to obtain additional polynucleotides that could be used in the claimed method. The ability to isolate novel polynucleotides is highly unpredictable and requires extensive experimentation. There is no specific guidance provided in the specification as to how use the cDNA of SEQ ID NO: 100 to obtain additional human telomerase gene products. The art teaches that human telomerase protein consists of 4 subunits. However, there is no disclosure in the specification as to how to predictably use the polynucleotide of SEQ ID NO: 100 to isolate additional polynucleotides encoding for other subunits of telomerase. The claims as broadly written further include methods for detecting any type of variant of SEQ ID NO: 100. However, there is no specific disclosure in the specification of variants of SEQ ID NO: 100 and it is highly unpredictable as to what would constitute such variants. Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims

must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the recitation of one c DNA molecules does not constitute a "representative number of DNA molecules" within the very large genus of all polynucleotides encoding human telomerase gene products. In addition, the state of the art indicates that the isolation of novel genes is achieved only through extensive trial and error experimentation. Accordingly, in view of the high level of unpredictability in the art and the lack of specific guidance and disclosure provided by the specification, undue experimentation would be required to practice the invention as it is broadly claimed.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by Chong (Science 91995) 270: 1663-1667).

It is noted that parent application 08/724,643 does not disclose probes and methods for the detection of polynucleotides encoding human telomerase cDNA and therefore the instant application is not entitled to priority to the filing date of 10/1/96.

Chong discloses a cDNA encoding human telomerase protein (see page 1666). The reference further teaches methods for detecting mRNA encoding human telomerase wherein said methods comprise hybridizing a human telomerase cDNA probe to sample mRNA and wherein hybridization of the cDNA probe to the sample mRNA is indicative of the presence of a polynucleotide (mRNA) encoding human telomerase (page 1664).

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Collins (U.S. Patent No. 5,770,422).

Collins teaches isolated polynucleotides which encode for human telomerase protein (see, for example, col. 5 and SEQ ID NO: 3). Collins further teaches methods for specifically detecting telomerase cDNAs using nucleic acid hybridization probes or amplification primers (col. 5-6). The reference teaches that human telomerase hybridization probes are useful in identifying wild-type and mutant human telomerase alleles in clinical and laboratory samples (col. 6). Collins does not specifically exemplify methods in which telomerase polynucleotides are detected. However, in view of the teachings of Collins of isolated telomerase cDNAs and of cDNA sequences useful as probes and primers and the suggestion of Collins to use such probes and primers for the detection of telomerase polynucleotides, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have generated a nucleic acid hybridization or amplification method for the specific detection of human telomerase polynucleotides in order to have achieved the benefit specifically disclosed by Collins of obtaining a method useful for identifying wild-type and mutant human telomerase nucleic acids.

6. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cao (U.S. Patent No. 5,747,317).

Cao teaches isolated polynucleotides which encode for human telomerase protein (see, for example, col. 2 and SEQ ID NO: 3). Cao further teaches methods for specifically detecting telomerase cDNAs using nucleic acid hybridization probes or amplification primers (col. 5-6).

The reference teaches that human telomerase hybridization probes are useful in identifying wild-type and mutant human telomerase alleles in clinical and laboratory samples (col. 6). Cao does not specifically exemplify methods in which telomerase polynucleotides are detected. However, in view of the teachings of Cao of isolated telomerase cDNAs and of cDNA sequences useful as probes and primers and the suggestion of Cao to use such probes and primers for the detection of telomerase polynucleotides, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have generated a nucleic acid hybridization or amplification method for the specific detection of human telomerase polynucleotides in order to have achieved the benefit specifically disclosed by Cao of obtaining a method useful for identifying wild-type and mutant human telomerase nucleic acids.

7. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington (U.S. Patent No. 5,981,707).

Harrington teaches isolated polynucleotides which encode for human telomerase protein (see, for example, col.2, and 23-25 and SEQ ID NO: 1). Harrington further teaches that telomerase nucleic acids are useful as hybridization probes for qualitatively or quantitatively detecting telomerase DNA or RNA in tissue or bodily fluid samples (col. 15). Harrington does not specifically exemplify methods in which telomerase polynucleotides are detected. However, in view of the teachings of Harrington of isolated telomerase cDNAs and of cDNA sequences useful as hybridization probes and the suggestion of Harrington to use such probes for the detection of telomerase polynucleotides, it would have been obvious to one of ordinary skill in the

art at the time the invention was made to have generated a nucleic acid hybridization or amplification method for the specific detection of human telomerase polynucleotides in order to have achieved the benefit specifically disclosed by Harrington of obtaining a method useful for qualitatively or quantitatively detecting the presence of human telomerase DNA or RNA.

8. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakayama (meeting held December 7-11, 1996; abstract 1662, page 286A, Molecular Biology of the Cell (Dec 1996).

Nakayama discloses a method for isolating a cDNA encoding a component of the human telomerase protein. It is stated that a cDNA was isolated which encodes for a long open reading frame. The human telomerase cDNA was used to synthesize recombinant protein and an affinity purified antibody against the recombinant protein was found to be capable of precipitating a protein fraction having telomerase activity. Nakayama does not specifically teach methods in which telomerase cDNA is used to detect polynucleotides encoding telomerase. However, it was conventional in the art at the time the invention was made to use newly isolated cDNAs to specifically detect DNA and mRNA corresponding to the cDNA in order to further characterize the newly isolated cDNA. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the cDNA of Nakayama in a nucleic acid hybridization method for the detection of polynucleotides encoding human telomerase in order to have achieved the benefit of obtaining a method useful for detecting the presence of or quantifying

DNA and mRNA encoding human telomerase which would be aid in the further characterization of the expression and activity of human telomerase.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

NCI-CGAP (GenBank Accession No. AA281296; 4/2/97) discloses a cDNA clone isolated from a human cDNA library. The cDNA consists of a 389 bp fragment which is contained within instantly disclosed SEQ ID NO: 1. However, NCI-CGAP does not characterize the cDNA as encoding a portion of the human telomerase protein. Accordingly, the prior art does not teach or suggest using the disclosed cDNA in methods for detecting a polynucleotide encoding a human telomerase gene product wherein the formation of a hybridization complex between said polynucleotide and a probe which specifically binds said polynucleotide is indicative of the presence of a polynucleotide encoding a human telomerase gene product.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. The fax number for the Technology Center is (703)-305-3014 or (703)-305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

July 11, 2000

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER